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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/598,468	08/31/2006	John S. Yu	67789-089US0	5815
50670	7590	03/21/2011	EXAMINER	
DAVIS WRIGHT TREMAINE LLP/Los Angeles 865 FIGUEROA STREET SUITE 2400 LOS ANGELES, CA 90017-2566				MACFARLANE, STACEY NEE
ART UNIT		PAPER NUMBER		
1649				
			NOTIFICATION DATE	DELIVERY MODE
			03/21/2011	ELECTRONIC

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patentlax@dwt.com  
sethlevy@dwt.com

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	10/598,468	YU ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	STACEY MACFARLANE	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

1) Responsive to communication(s) filed on 28 December 2010.

2a) This action is **FINAL**.                            2b) This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

4) Claim(s) 1,4,6-11,13,16,18,22,24-32,34-36 and 38 is/are pending in the application.

4a) Of the above claim(s) 4,10,11,13,16,18 and 22-32 is/are withdrawn from consideration.

5) Claim(s) \_\_\_\_\_ is/are allowed.

6) Claim(s) 1, 6-9, 34-36 and 38 is/are rejected.

7) Claim(s) \_\_\_\_\_ is/are objected to.

8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

9) The specification is objected to by the Examiner.

10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) All    b) Some \* c) None of:

1. Certified copies of the priority documents have been received.
2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)	4) <input type="checkbox"/> Interview Summary (PTO-413)
2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)	Paper No(s)/Mail Date. _____ .
3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)	5) <input type="checkbox"/> Notice of Informal Patent Application
Paper No(s)/Mail Date _____ .	6) <input type="checkbox"/> Other: _____ .

## DETAILED ACTION

### ***Response to Amendment***

1. Claims 2, 3, 5, 12, 14, 15, 17, 19-21, 23, 33, 37, 39-43 are cancelled; Claims 1, 4, 6, 13, 18, 24 and 34 have been amended as requested in the amendment filed on December 28, 2010. Following the amendment, claims 1, 4, 6-11, 13, 16, 18, 22, 24-32, 34-36 and 38 are pending in the instant application.

Claims 4, 10, 11, 13, 16, 18 and 22-32 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim.

Claims 1, 6-9, 34-36 and 38 are under examination in the instant office action.

### ***Claim Rejections - 35 USC § 103(New Necessitated by Amendment)***

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

3. As currently amended to require the NSC of the claims to express a heterologous gene comprising a polypeptide that is therapeutic for the treatment of a disease condition including glioblastoma multiforme, Claims 1, 6-9, 34-36 and 38 are rejected under 35 U.S.C. 103(a) as obvious over Luo et al., (2002), as evidenced by Markagakis

et al., (2003), and further in view of Bradbury, *The Lancet*, 360:1226, published online October 18, 2002.

The combined teachings of the references demonstrate that there are subpopulations of neural stem cells that express the claimed elements required for cell selection, and said cells can be engineered to produce IL-12 for the treatment of glioma tumors.

Luo et al. teach stem cells isolated from the neural tube or neuroepithelium, are either A2B5+ glial-restricted progenitor cells or NCAM+ neuron-restricted progenitors. Luo et al. teach that both CXCR4 and SDF-1 genes are expressed in only in the A2B5 positive glial-restricted progenitor cells (Table 3). The Maragakis et al. art is relied upon as evidence that it was well-known within the art that glial-restricted progenitor cells differentially express glutamate receptors as they progress along the continuum from glial precursor to astrocyte precursor to differentiated astrocyte: EAAT2 being not expressed in *any* of the precursors (Abstract and Figure 2B); and EAAT1 being only expressed upon a shift along the astrocyte lineage (Figure 2A and page 138, paragraph bridging columns).

Thus, the Luo and Maragakis teach that isolated A2B5+ NSCs that exhibit CXCR4, are responsive to SDF-1 but which do not express EAAT1 or EAAT2, were known in the art. Luo, evidenced by Maragakis, is silent with respect to these NSCs expressing a heterologous gene, namely IL-12 of instant claim 9. The Bradbury et al. prior art, however, teaches that prior to filing it was known in the art that *in situ* IL-12 conferred potent cytotoxic immunity against glioma. The reference further teaches that

NSCs track to intracranially injected glioma cells and NSCs could be engineered to produce IL-12. The publication reports that treatment with IL-12-expressing NSCs was therapeutic for glioma injected mice relative to untreated.

It would have been obvious to one of ordinary skill in the art to modify the isolated NSCs exhibiting CXCR4, affinity for SDF-1, expressing the A2B5 marker and not expressing EAAT1 or EAAT2 as taught by Luo and Maragakis, with the heterologous gene for IL-12 as taught by Bradbury. A skilled artisan would have been motivated to do so because the Bradbury et al. prior art explicitly teaches that NSCs in situ confers long-lasting cytotoxic immunity against glioma and that NSCs can be engineered to produce IL-12.

Therefore, the invention as a whole is *prima facie obvious* and Claims 1, 6-9, 34-36 and 38 are rejected

Applicants arguments filed 12/28/10 are moot in view of the new ground of rejection.

### ***Conclusion***

4. No claim is allowed.
5. This application contains claims drawn to an invention nonelected with traverse in Paper filed on March 27, 2009. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.
6. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP

§ 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to STACEY MACFARLANE whose telephone number is (571)270-3057. The examiner can normally be reached on M-R 5:45 to 3:30, TELEWORK-Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker can be reached on (571) 272-0911. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Stacey MacFarlane  
Examiner  
Art Unit 1649

/Lorraine Spector/  
Primary Examiner, Art Unit 1647